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Electronic Supplementary Information(ESI)

Synthesis of 4a-carba-α-D-lyxofuranose from isopropyloxy-2,3-*O*-isopropylidene-L-erythruronolactone *via* Tebbe mediated cascade reaction

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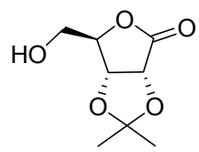
Experimental section

General information: All reactions are carried under nitrogen atmosphere in oven dried glassware equipped with a magnetic stirrer and a rubber septum unless otherwise indicated. All solvents are freshly distilled before use; THF over sodium and benzophenone; DCM over calcium hydride. All other commercial reagents were used without further purification, unless otherwise noted. Reactions were monitored by thin layer chromatography (TLC) of aliquots using glass sheets coated (0.25 mm layered thickness) with silica gel F_{254} (Merck Kiesel gel 60). TLC plates are viewed under UV light and charred with phosphomolybdic acid. Column chromatographies were carried out with silica gel 60-120 mesh (Merck). ^{1}H and ^{13}C NMR spectra were recorded in deuterated solvents, on Bruker Avance 300 MHz Spectrometer. IR spectra were recorded with a Thermo Nicolet nexus 670 FT-IR spectrometer. HRMS were obtained on a Q STAR XL HYBRID (PE SEIEX) analytical instrument. Optical rotations were measured with Horiba-SEPA-300 digital polarimeter. Melting points were recorded on a FISHER JOHNS melting point apparatus.

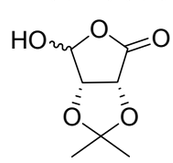
2,3-*O*-isopropylidene-D-ribono-γ-lactone (8).



8

To a solution of 2,3–*O*–isopropylidene–D–ribose **(7)** (2.0 g, 10.52 mmol) in water (25 mL) was added $BaCO_3$ (12.88 g, 65.26 mmol) at 0° C. To this reaction mixture, bromine (1.62 ml, 31.58 mmol) was added for a period of 30 min at 0°C, allowed to stir for 1 h at the same temperature. After completion of the reaction 10% hypo solution (10 mL) was added to quench the excess bromine at 0° C. Reaction mixture was filtered and passed through a pad of celite and extracted with $CHCl_3$ and the extract was washed with water, brine, dried over anhy. Na_2SO_4 and concentrated to give a residue. Purification of the residue on silica gel (elution with 50% ethyl acetate in hexanes) afforded 1.30 g (66%) of **8** as a white solid: Mp 177–180° C; $[\alpha]^{20}_{D}$ 62.4 (*c* 0.79, $CHCl_3$)^{20}; IR (KBr) ν_{max} 3468, 2991, 1775, 1389, 1201, 1079 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 3H), 1.5 (s, 3H), 2.92 (t, 1H, *J* = 4.84 Hz), 3.8 (m, 1H), 4.0 (m, 1H), 4.64 (s, 1H), 4.85 (d, 2H, *J* = 5.81 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.4, 26.6, 61.8, 75.6, 78.2, 82.9, 113.1, 175.2; MS (EI): m/z 173 (M–15); MS (ESI): (188); HRMS (ESI) m/z calcd 211.0582, found 211.0577;

(3a,6a*S*)-6-hydroxy-2,2-dimethylperhydrofuro(3,4-d) (1,3) dioxol-4-one (9).

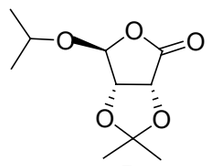


9

To the solution of **8** (1.2 g, 6.38 mmol) and NaOH (0.25 g, 6.38 mmol) in water (20 mL) was heated at 40°C until all the solid material dissolved. The reaction mixture was then cooled to 0° C, and $NaIO_4$ (1.36 g, 6.38 mmol) in water (2 mL) was added drop wise at 0°C. The reaction mixture was allowed to stir for 15 min, then $BaCl_2$ (0.6 g) was added and the resulting precipitate was acidified to pH 3 with 2 N HCl and

extracted with EtOAc. The extract was washed with water, brine, dried over anhy. Na_2SO_4 and concentrated in *vacuo*. The solid obtained was recrystalized in ethyl acetate to give (**9**) as a white solid (2.08 g, 72%) : Mp 100–102°C; $[\alpha]^{20}_D$ -21.341 (*c* 1.0, $CHCl_3$); IR (KBr) ν_{max} 3412, 1756, 1383, 1080 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$), 1.41 (s, 3H), 1.53 (s, 3H), 4.68 (d, 1H, *J* =5.63 Hz), 4.91 (d, 1H, *J* = 5.34 Hz), 5.87 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$ + DMSO) δ 24.0, 25.1, 73.3, 78.9, 98.3, 111.9, 172.4; MS (LCMS) m/z calcd for $[M+H]^+$ 175, found 175;

(3a*R*,6a*S*)-6-isopropoxy-2,2-dimethylperhydrofuro(3,4-d)(1,3)dioxol-4-one (5).

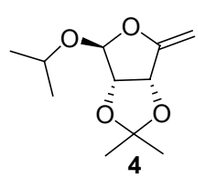


5

To the solution of lactol **9** (0.75 g, 4.31 mmol) in anhydrous 2-propanol (20 mL), PPTS (0.11 g, 0.43 mmol) was added. Reaction mixture was refluxed at 80° C for a period of 1.5 h. After completion of the reaction, reaction mixture was concentrated to a syrup in *vacuo*, which was then dissolved in 50 mL of EtOAc, washed with water, brine, dried using anhy. Na_2SO_4 and concentrated in *vacuo* to give a residue. Purification of the residue on silica gel (elution with 10% ethyl acetate in hexane) afforded **5** as a light yellow oil (0.63 g, 84%) : $[\alpha]^{20}_D$ +45.6 (*c* 0.42, $CHCl_3$); IR (KBr) ν_{max} 2983, 1795, 1380, 1108, 929, 771 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 1.22 (d, 3H, *J* = 4.46 Hz), 1.24 (d, 3H, *J* = 4.46 Hz), 1.37 (s, 3H), 1.45 (s, 3H), 4.03 (septet, 1H, *J* = 5.94 Hz), 4.48 (d, 1H, *J* = 5.2 Hz), 4.76 (d, 1H, *J* = 5.2 Hz), 5.4 (s,1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 21.2, 23.0, 25.6, 26.6, 72.3, 74.5, 79.7, 102.2, 114.1, 173.3; HRMS (ESI) m/z calcd for $C_{10}H_{17}O_5$ 217.1015, found 217.1078.

(3as,4S,6aR)-4-isopropoxy-2,2-dimethyl-6-methylene-tetrahydrofuro[3,4-d][1,3]dioxole(4)

(Reaction with 1eq of Tebbe reagent)



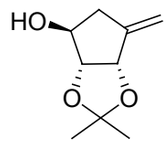
4

To the solution of lactone **5** (0.15 g, 0.69 mmol) in dry THF (10 mL), Tebbe reagent (1.49 mL, 0.69 mmol, 0.5 M solution in toluene) was added at 0° C. (Stirring continued for a period of 1 h. at 0°C). After being stirred for 1 h. at 0°C the reaction mixture was quenched by adding 10% aq NaOH solution(1.2 mL) for a period of 10 min. Precipitate was filtered through a pad of celite, washed with EtOAc. Filtrate and washings were combined and washed with water, brine, dried (Na_2SO_4), concentrated in *vacuo* to give a residue . Purification of the residue on silica gel (elution with 2-3% ethyl acetate in hexane) afforded (0.027 g, 18.2%) compound **4** as a light yellow oil: $[\alpha]^{20}_D$ + 8 (*c* 0.1, $CHCl_3$); IR (KBr) ν_{max} 761, 1216, 1463, 1232, 2855, 2924 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.18 (d, 6H, *J* = 6.04 Hz), 1.32 (s, 3H), 1.44 (s,

3H), 3.91 (multiplet, 1H), 4.29(s, 1H), 4.41(d, 1H, *J* = 6.04 Hz), 4.48 (s, 1H), 4.97 (d, 1H, *J* = 6.04 Hz), 5.25 (s, 1H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 21.49, 23.28, 25.57, 26.7, 70.4, 78.84, 83.01, 88.18, 105.67, 113.0, 161.15; HRMS(ESI) m/z calcd for $[C_{11}H_{18}O_4+H]^+$ 215.1278, found 217.1281. Compound **1** (0. 017g,13%) and startimg material **5** (0.025 g, 17%) were also isolated.

(3a*R*,4*S*,6a*S*)-2,2-dimethyl-6methyleneperhydrocyclopenta[d][1,3]dioxol-4-ol (1)

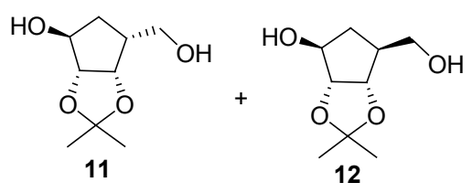
(Reaction with 2 eq of Tebbe reagent)



1

To the solution of lactone **5** (0.1 g, 0.48 mmol) in dry THF (10 mL), Tebbe reagent (2. 2mL, 1.06 mmol, 0.5 M solution in toluene) was added at 0° C. (Stirring continued for a period of 1 h. at 0°C). After being stirred for 1 h. at 0°C the reaction mixture was quenched by adding 10% aq NaOH solution(2 mL) for a period of 10 min. Precipitate was filtered through a pad of celite, washed with EtOAc. Filtrate and washings were combined and washed with water, brine, dried (Na_2SO_4), concentrated in *vacuo* to give a residue . Purification of the residue on silica gel (elution with 20–25% ethyl acetate in hexane) afforded (0.032 g, 40%) compound **1** as a light yellow oil: $[\alpha]^{20}_D$ -125.24 (*c* 2.67, $CHCl_3$); IR (KBr) ν_{max} 2935, 1375, 1219, 1041, 772 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.3 (s, 3H), 1.41 (s, 3H), 1.42–1.45 (brs, 1H), 2.17 (d, 1H, *J* = 15.11 Hz), 2.77–2.88 (m, 1H), 4.15 (d, 1H, *J* = 4.53 Hz), 4.38 (d, 1H, *J* = 5.29 Hz), 4.78 (d, 1H, *J* = 6.04 Hz), 5.17 (s, 1H), 5.28 (s, 1H); ^{13}C NMR (50 MHz,$CDCl_3$) δ 24.1, 26.3, 38.1, 74.3, 81.2, 86.0, 110.9, 114.3, 147.6; HRMS(ESI) m/z calcd for [$(C_9H_{14}O_3F)^+$] 189.0926, found 189.0928.

(3a*R*,4*S*,6*R*,6a*S*)-6-(hydroxymethyl)-2,2-dimethylperhydrocyclopenta[*d*][1,3]dioxol-4-ol(11), and (3a*R*,4*S*,6*S*,6a*S*)-6-(hydroxymethyl)-2,2-dimethylperhydrocyclopenta[*d*][1,3]dioxol-4-ol (12)

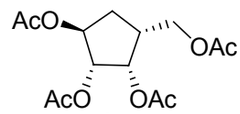


11 **12**

To the soluion of **1** (0.1 g, 0.51 mmol) in THF (10 mL), $BH_3.Me_2S$ (0.16 mL, 1.55 mmol) was added drop wise at –10° C. Stirrring continued for 16 h at room temperature. After which time NaOH (3N, 1.3 mL) follwed by (30%) H_2O_2 (2.2 mL) solution were added at 0°C and stirring continued for 30 min at the same temperature. The reaction mixture was diluted with EtOAc, washed with water, brine, dried using anhydrous Na_2SO_4 and concentrated in *vacuo* to give a residue. Purification of the residue on silica gel (elution with 50% ethyl acetate in hexane) afforded **11** (0.057 g, 53%) and **12** (0.028 g, 15%) as low melting solids. For compound **11**; mp 41–43° C; $[\alpha]^{20}_D$ (+) 38 (*c* 0.97, CH_2Cl_2)[8a]; IR (KBr) ν_{max} 3418, 2933, 1617, 1379,1210, 1059, 1019, 866, 518 cm^{-1} ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (s, 3H), 1.42 (s, 3H), 1.49 (bs, 1H), 1.61 (dd, 1H, *J* = 5.6 Hz, 13.3 Hz), 1.95 (dt, 1H, *J* = 4.0 Hz, 13.3 Hz), 2.23 (bs,1H), 2.39 (m, 1H), 3.7 (dd, 1H, *J* = 6.3 Hz, 11.4 Hz), 3.9 (dd, 1H, *J* = 4.0 Hz,11.4 Hz), 4.16 (d, 1H, *J* = 4.0 Hz), 4.36 (dd, 1H, *J* = 1.5 Hz, *J* = 5.6 Hz), 4.75 (t, 1H, *J* = 5.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.7, 25.9, 32.9, 42.4,

61.8, 75.3, 81.4, 86.7, 110.3; HRMS(ESI) m/z calcd. for [$(C_9H_{16}O_4Na)^+$] 211.0946, found 211.0953; For compound **12**; $[\alpha]^{20}_D$ -3.2 (c 0.625, CH_2Cl_2); (KBr) ν_{max} 3412, 2926, 2855, 1461, 1377, 1271, 1041, 864, 759 cm^{-1} ; ^1H NMR (200 MHz, $CDCl_3$) δ 1.26 (S, 3H), 1.39 (S, 3H), 1.54 (d, 1H, *J* = 13.67 Hz), 2.38 (m, 2H), 3.62 (dd, 1H, *J* = 2.34 Hz, 10.55 Hz), 3.8 (dd, 1H, *J* = 3.90 Hz, J = 10.55 Hz), 4.11 (d, 1H, *J* = 5.47 Hz), 4.35 (dd, 1H, *J* = 0.78 Hz, 5.47 Hz), 4.64 (d, 1H, *J* = 5.47 Hz); ^{13}C NMR (50 MHz, $CDCl_3$); δ 23.9, 26.5, 35.55, 47.2, 64.5, 76.8 , 83.9, 88.2, 109.7; HRMS(ESI) m/z cacd. for $[(C_9H_{16}O_4Na)^+]$ 211.0949, found 211.0946

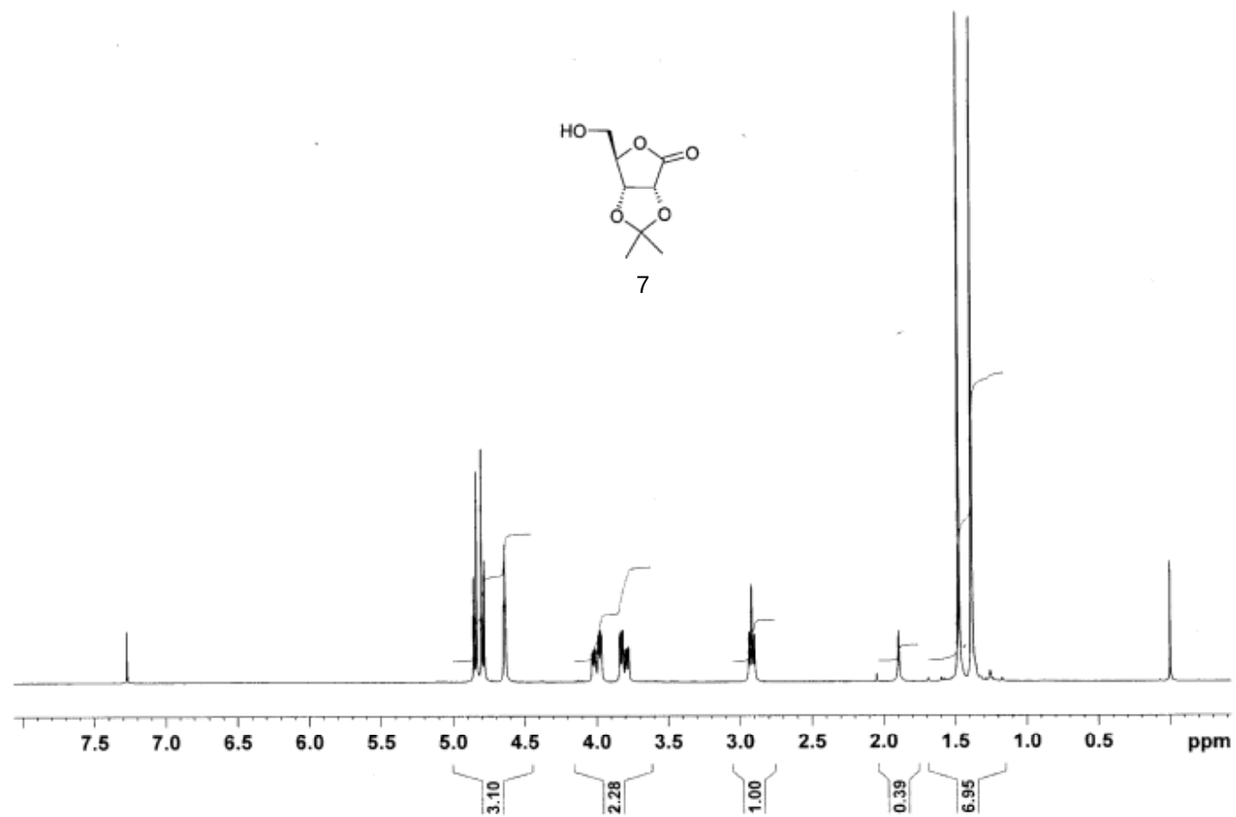
1,2,3,5-tetra-O-acetylcarba- α-D-lyxofuranose (14).



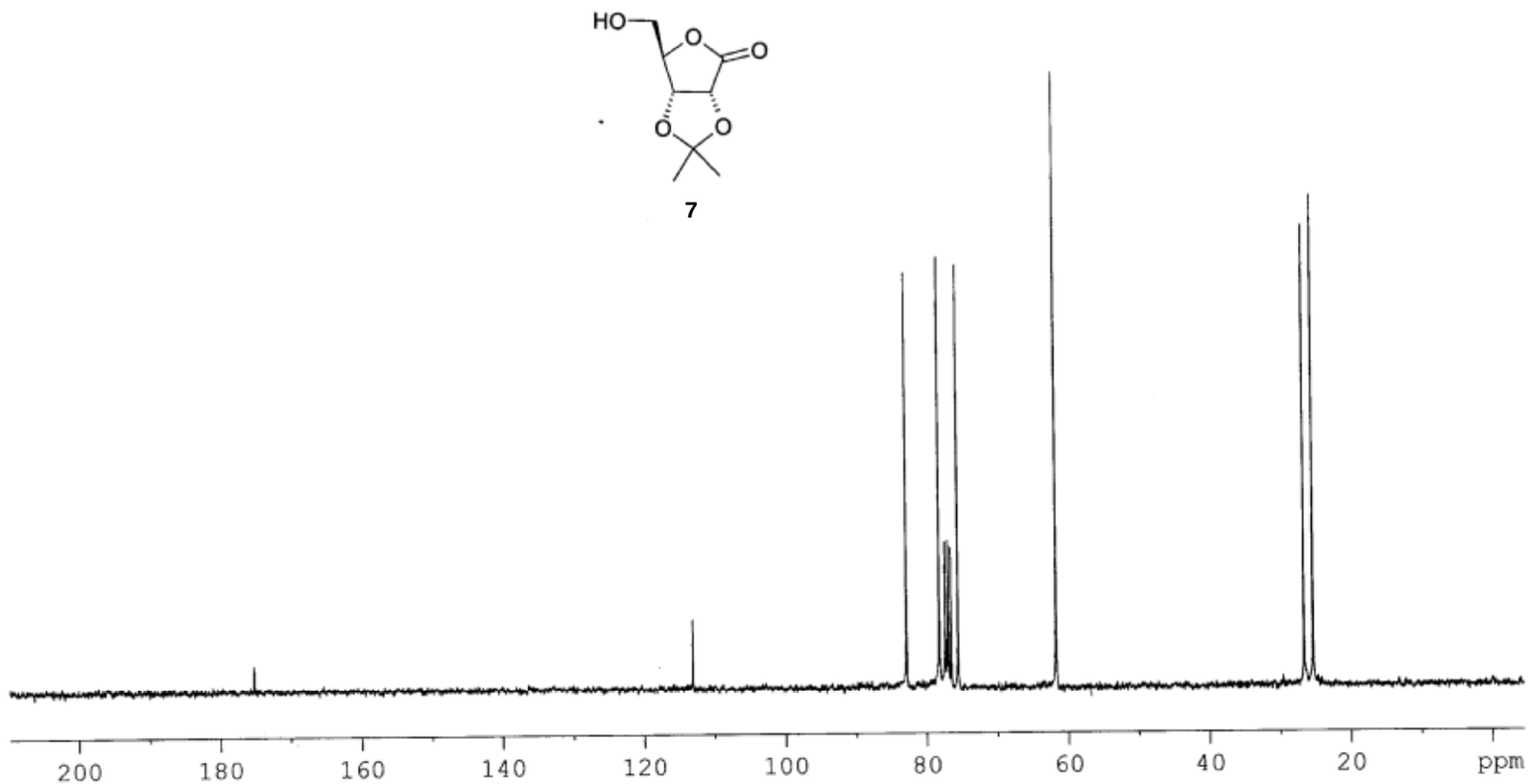
14

Diol **11** (0.05 g,) was treated with methanolic hydrochloric acid (MeOH/HCl, 5 mL) at 0° C for 15 min. The reaction mixture was concentrated in *vacuo* to remove all the solvent. The crude residue was dissolved in DCM (7 mL) and treated with triethyl amine (0.35 mL, 3.5 mmoles), acetic anhydride (0.25 ml, 2.7 mmols), and a few crystals of DMAP for 6 h at room temperature. Then methanol (1ml) was added, and stirring was continued for 15 min. Then solution was diluted with 0.1N HCl, the layers are separated, and the organic layer was washed with saturated aqueous $NaHCO_3$. The aqueous layer was re-extracted twice using DCM (10 mL × 2). The total organic extracts are combined and dried using anhydrous Na_2SO_4 and concentrated in *vacuo* to give a residue. Purification of the residue on silica gel (eluation with 22–25% ethyl acetate in hexanes) afforded **14** (0.098 g, 92%) as a yellow oil. $[\alpha]^{20}_D$ +32 (*c* 0.123, CH_2Cl_2); IR (KBr) ν_{max} 3466, 2924, 2854, 1742, 1437, 1369, 1226, 1036, 893, 761, 603 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.77 (m, 1H), 2.02 (S, 6H), 2.06 (S, 3H), 2.08 (S, 3H), 2.17(m, 1H), 2.68(m, 1H), 4.04 (2 dd, AB system, 2H, *J* = 6.6 Hz, 10.9 Hz, 8.4Hz, 10.9 Hz), 5.21 (m, 2H), 5.45 (t, 1H, *J* = 3.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$); δ 20.55 (2C), 20.69, 20.89, 31.88, 37.25, 62.39, 72.17, 75.33, 77.42, 169.84, 169.97, 170.47, 170.71; HRMS (ESI) m/z calcd. for $[(M\text{-}C_{14}H_{20}O_8Na)^+]$ 339.1058, found 339.1055.

^{1}H NMR OF COMPOUND 7 IN $CDCL_3$ (300 MHz)



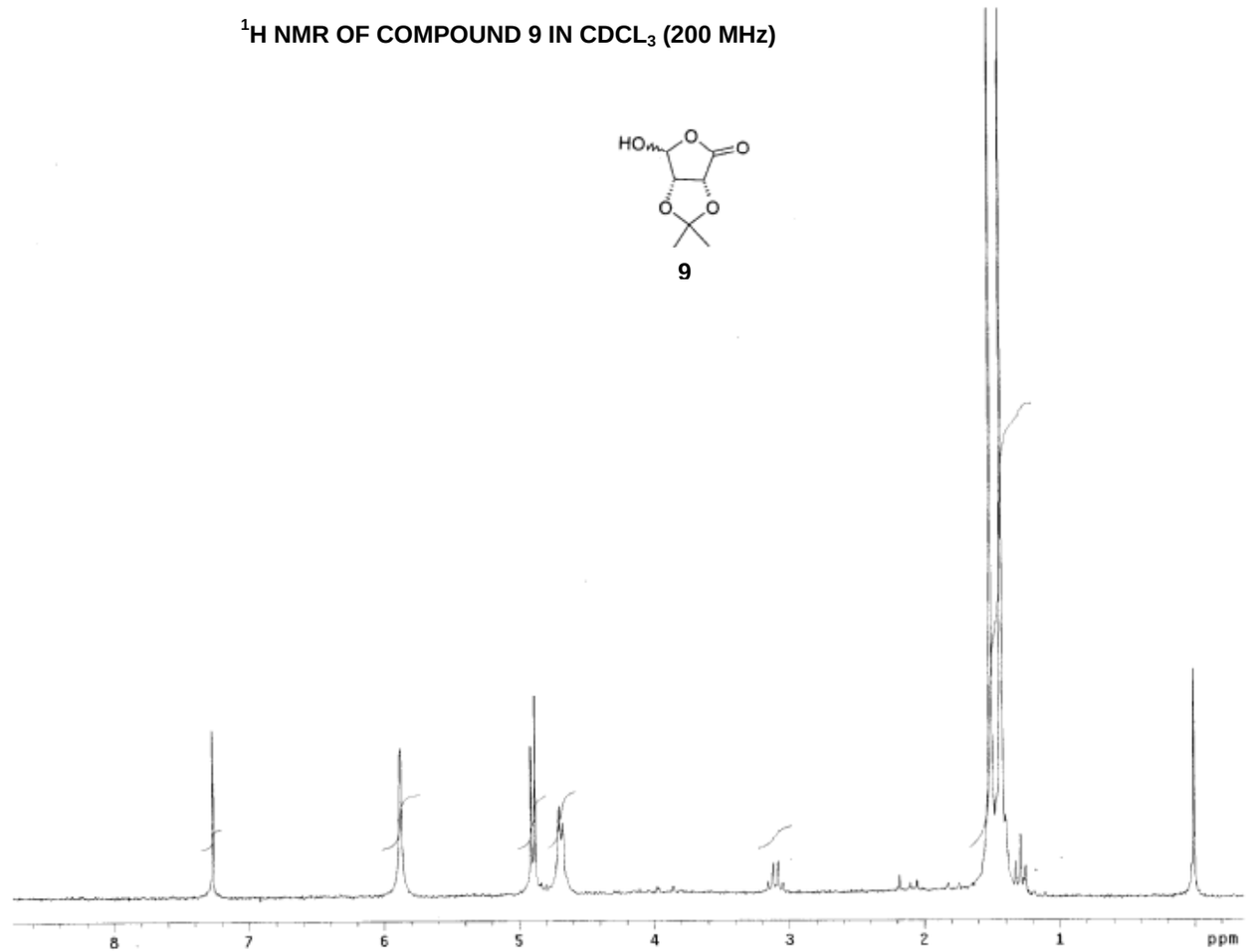
^{13} CNMR OF COMPOUND 7 IN $CDCL_3$ (75 MHz)



^{13}C NMR OF COMPOUND 7 IN $CDCL_3$ (75 MHz)

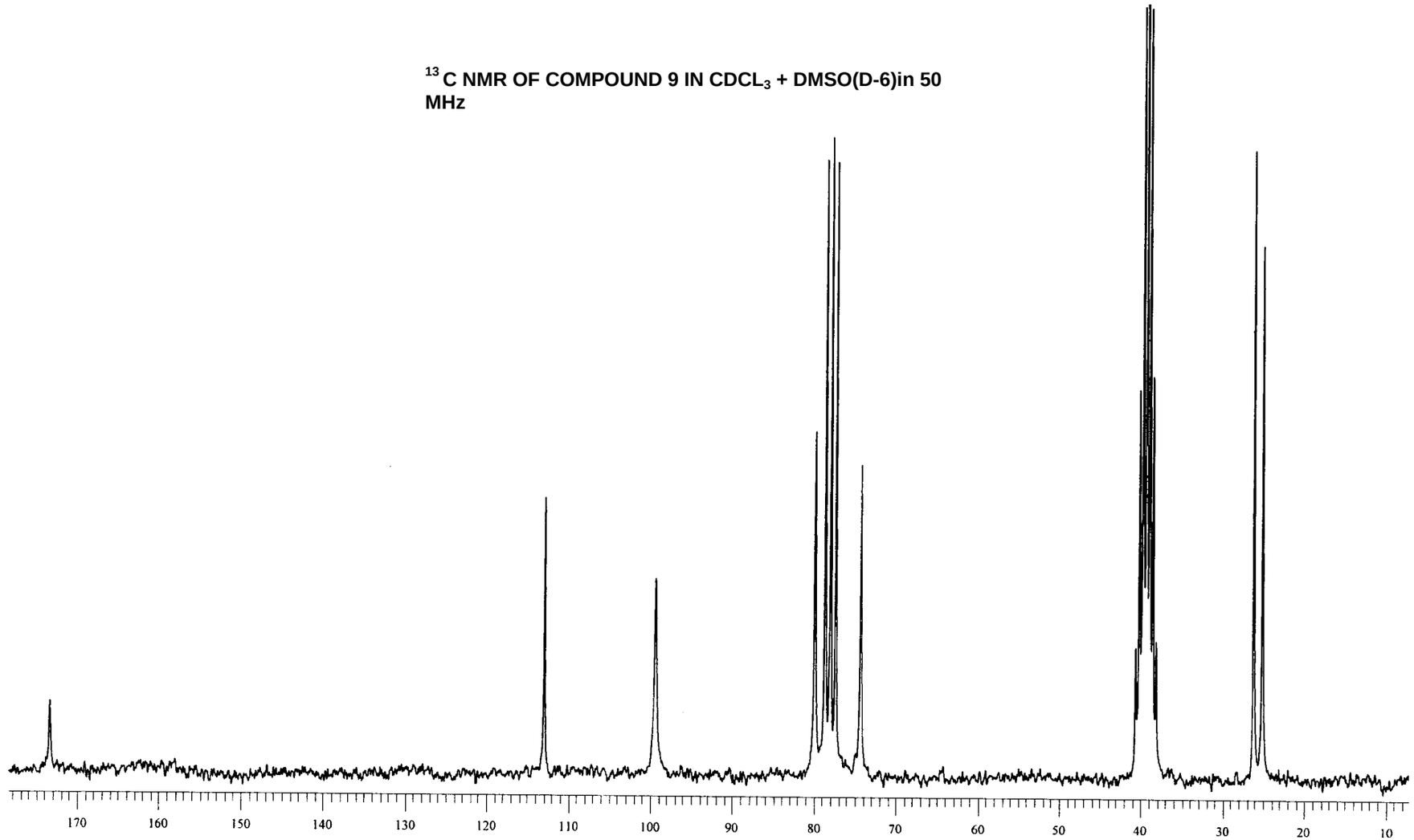
^{1}H NMR OF COMPOUND 9 IN $CDCL_3$ (200 MHz)

9



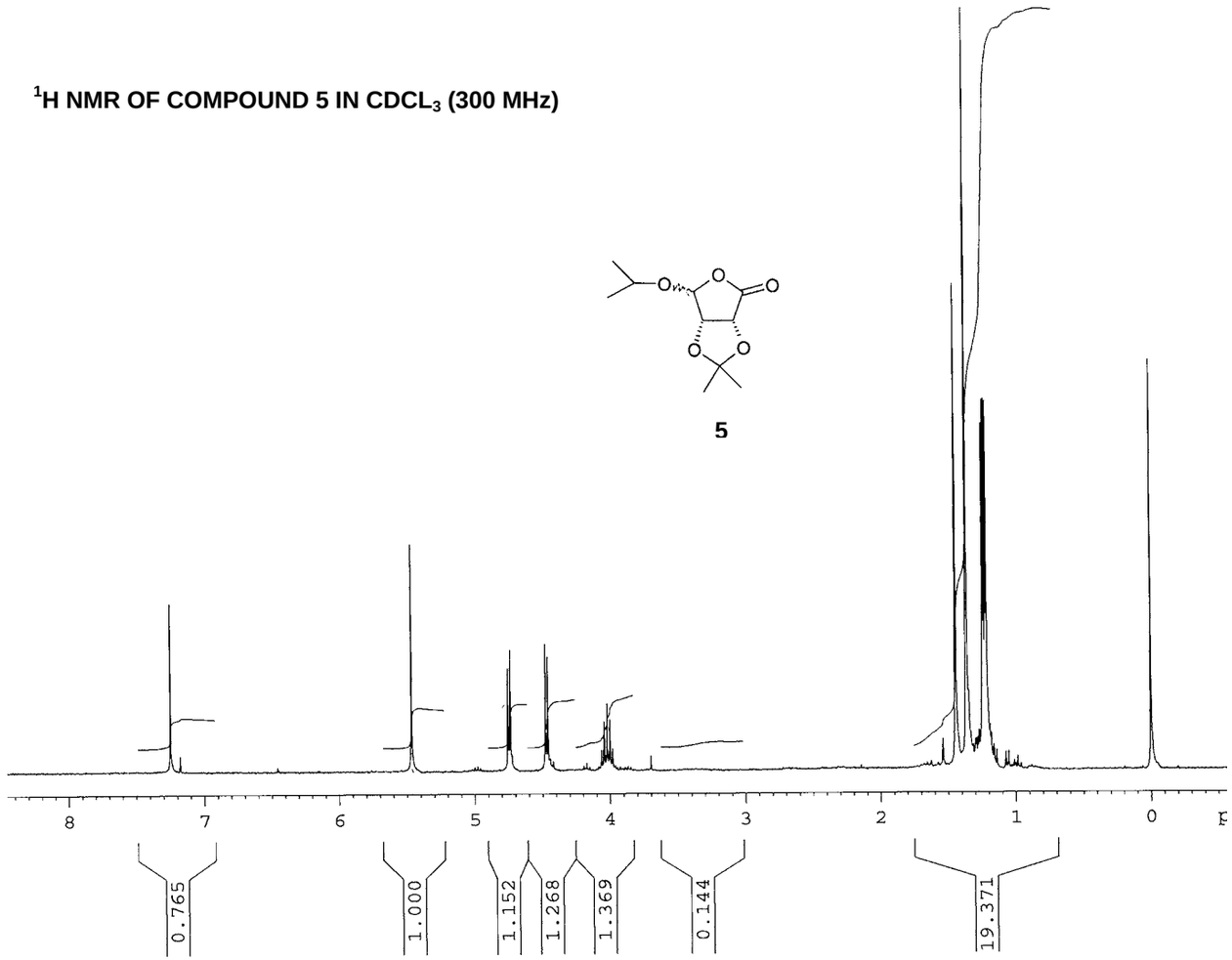
^{1}H NMR OF COMPOUND 9 IN $CDCL_3$ (200 MHz)

^{13}C NMR OF COMPOUND 9 IN $CDCL_3$ + DMSO(D-6)in 50 MHz

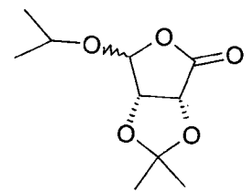


^{13}C NMR OF COMPOUND 9 IN $CDCL_3$ + DMSO(D-6)(50 MHz)

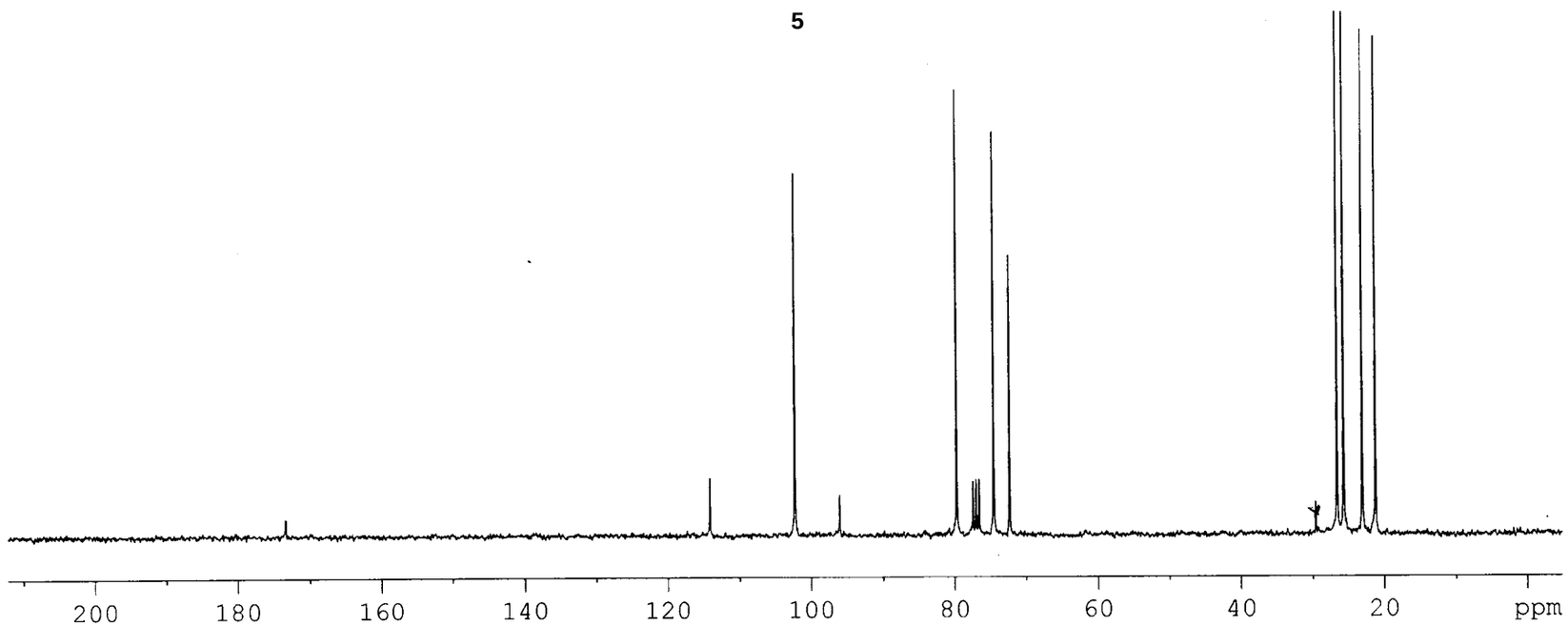
^{1}H NMR OF COMPOUND 5 IN $CDCL_3$ (300 MHz)



^{13}C NMR OF COMPOUND 5 IN $CDCL_3$ (75 MHz)

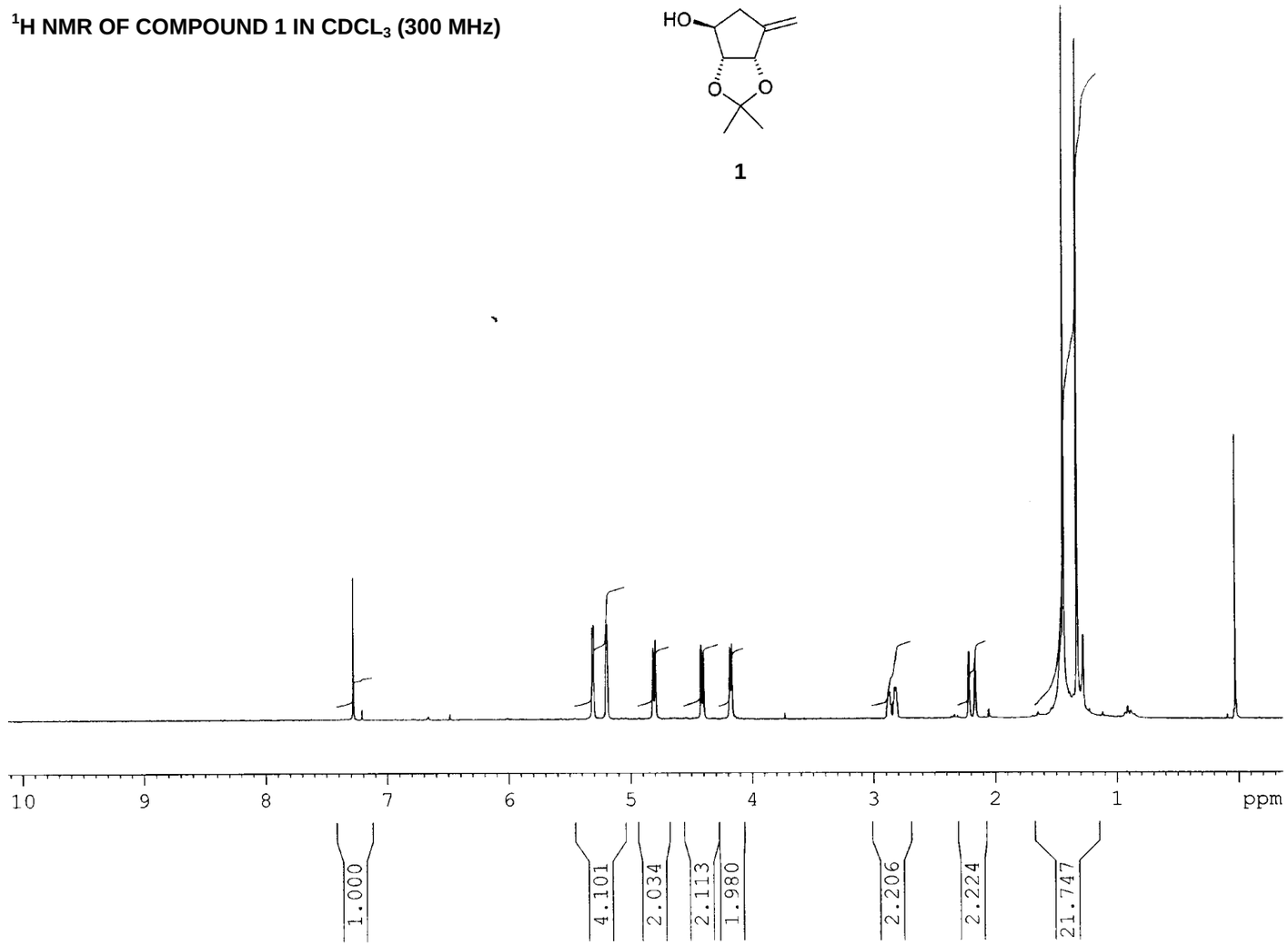


5

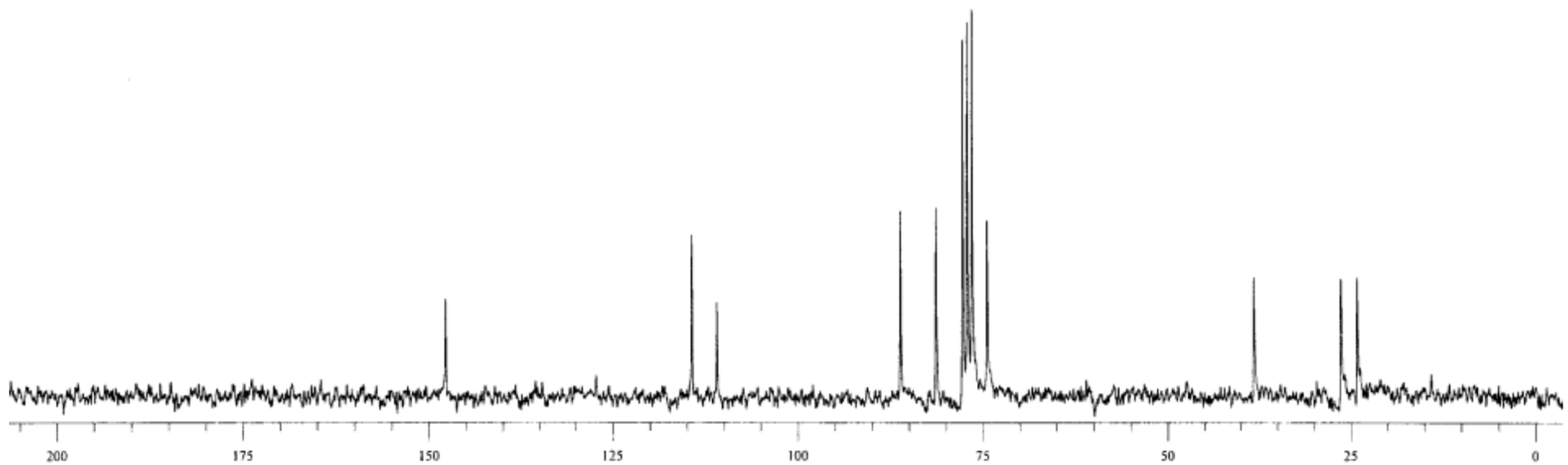


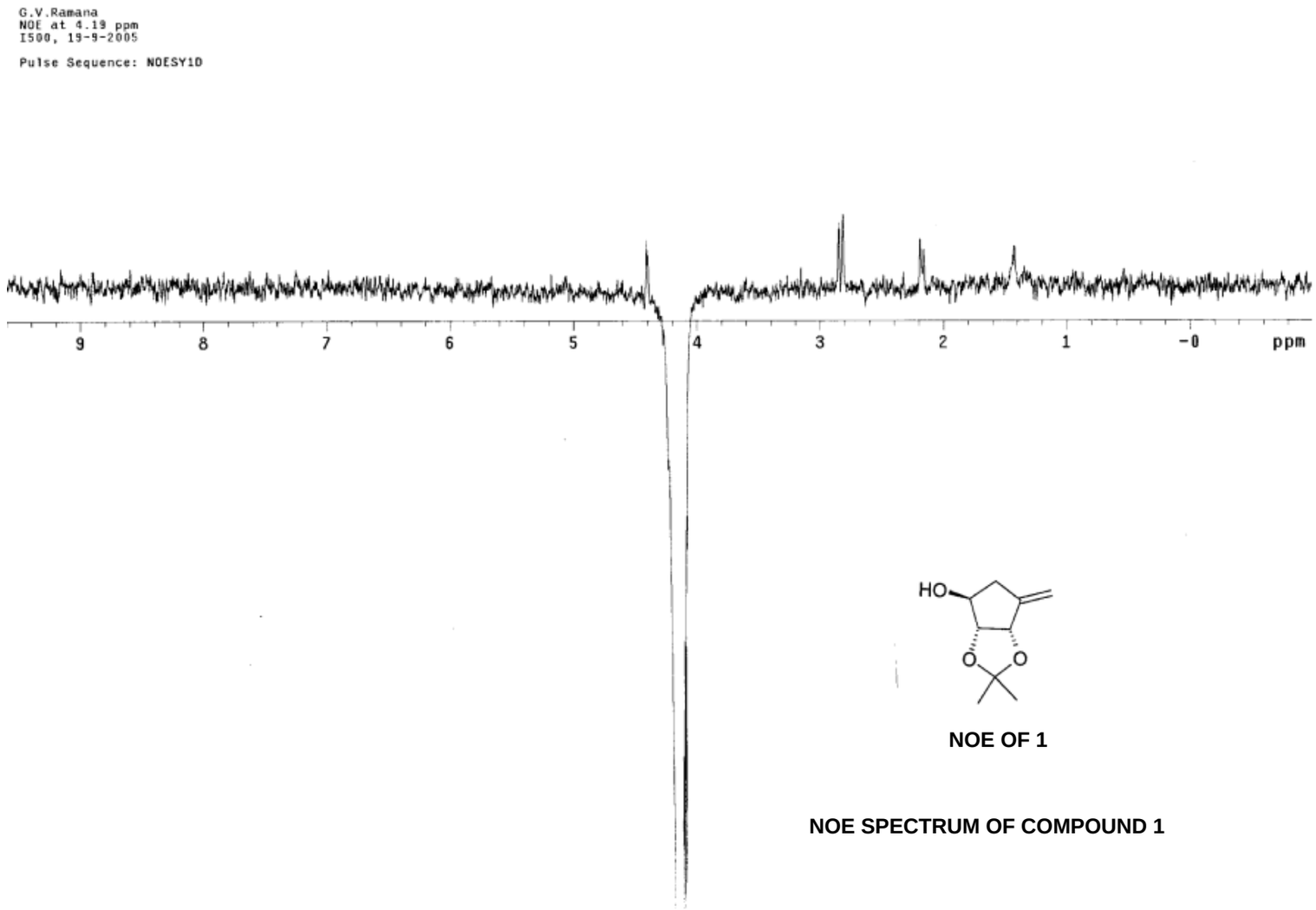
^{1}H NMR OF COMPOUND 1 IN $CDCL_3$ (300 MHz)

1



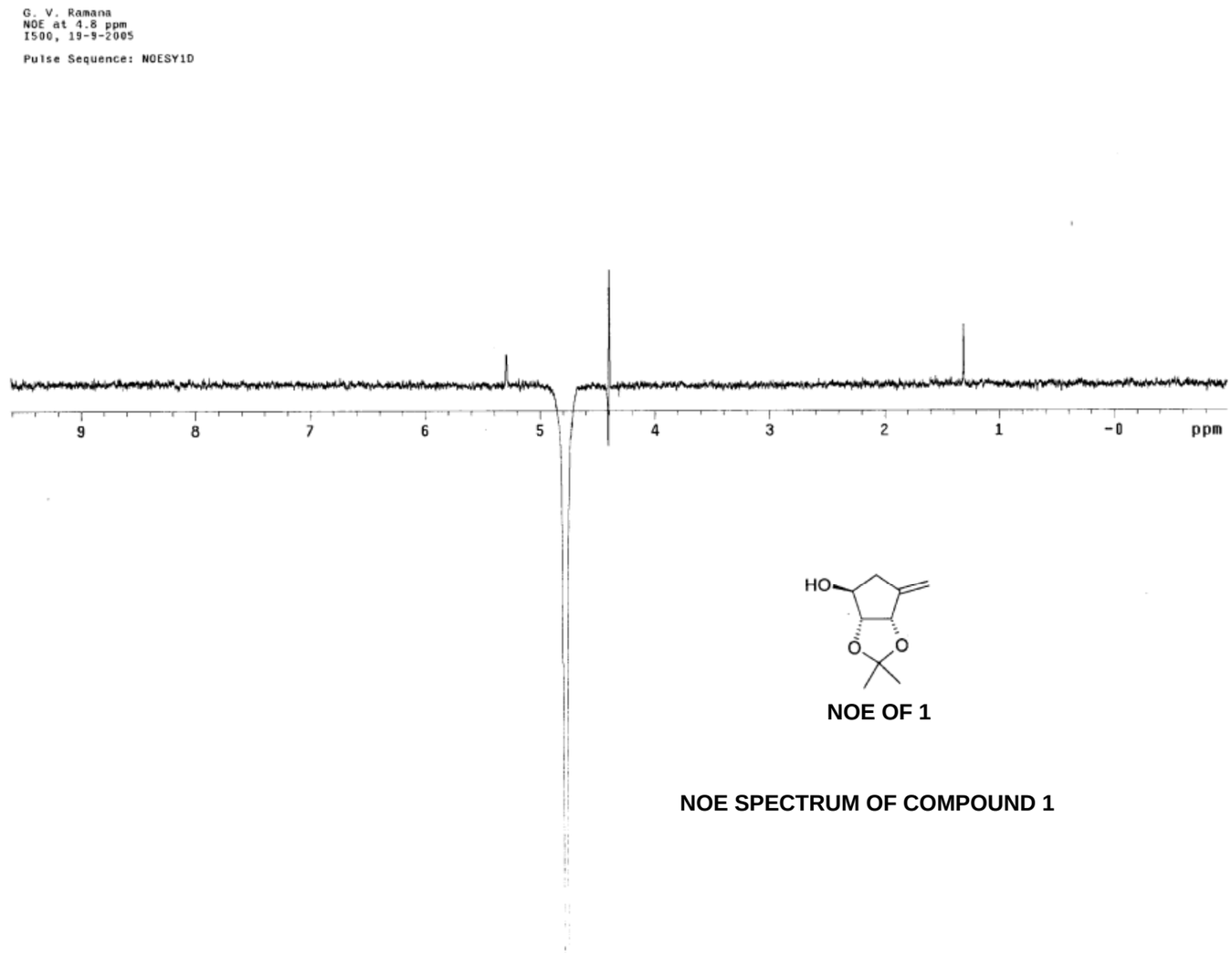
^{13}C NMR OF COMPOUND 1 IN $CDCL_3$ (50 MHz)





NOE OF 1

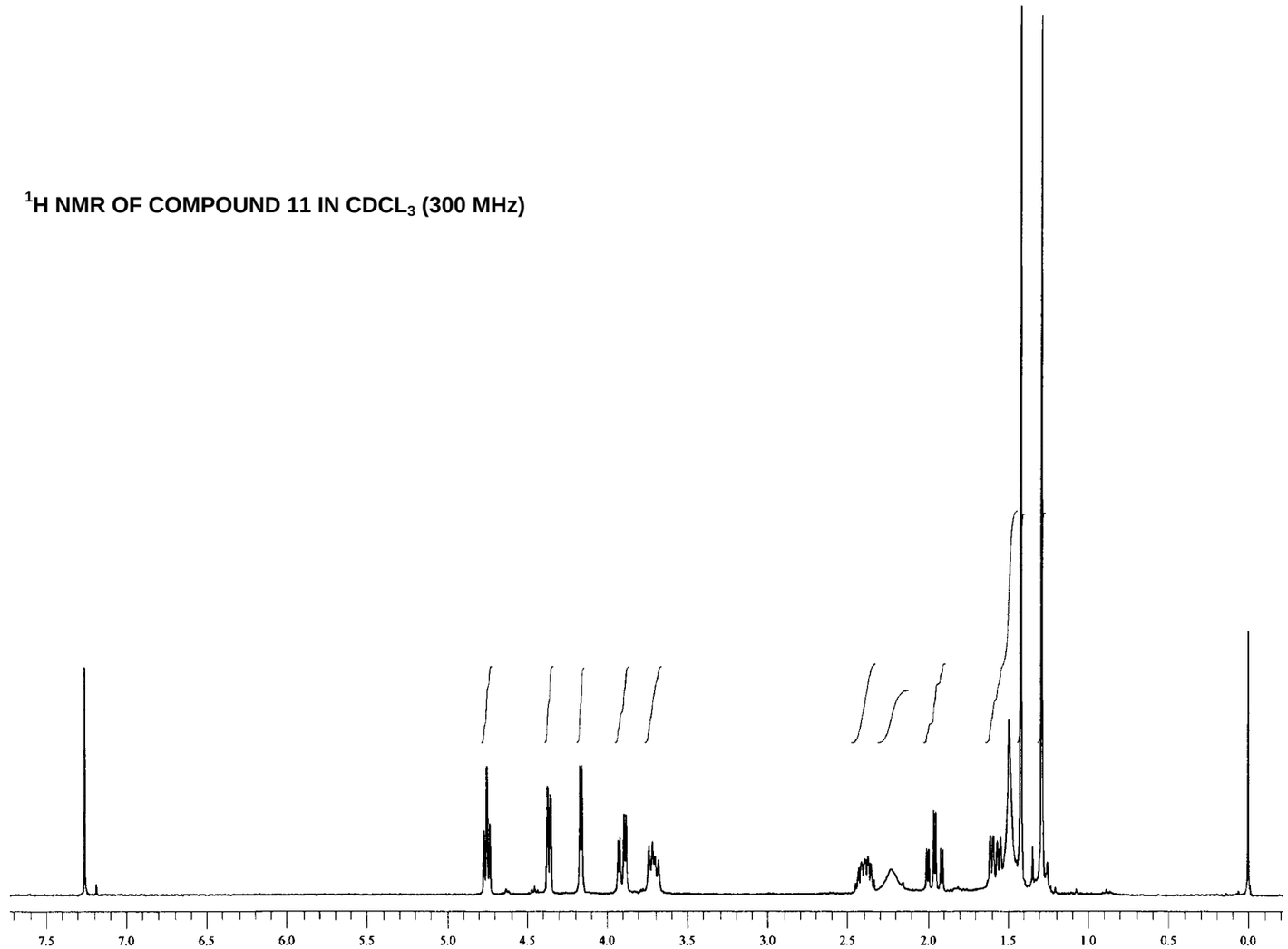
NOE SPECTRUM OF COMPOUND 1



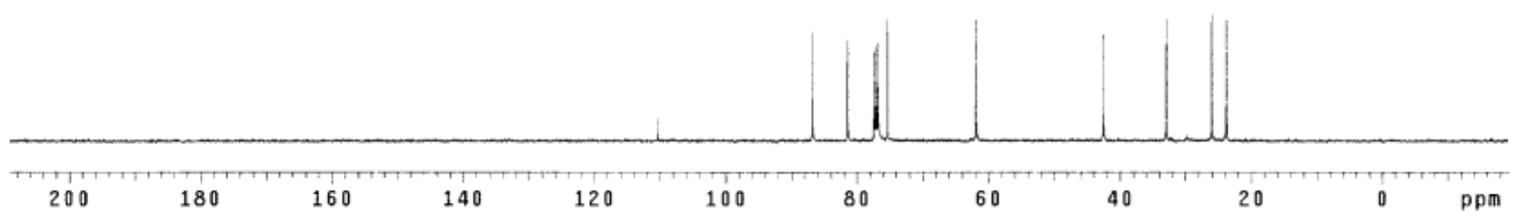
NOE OF 1

NOE SPECTRUM OF COMPOUND 1

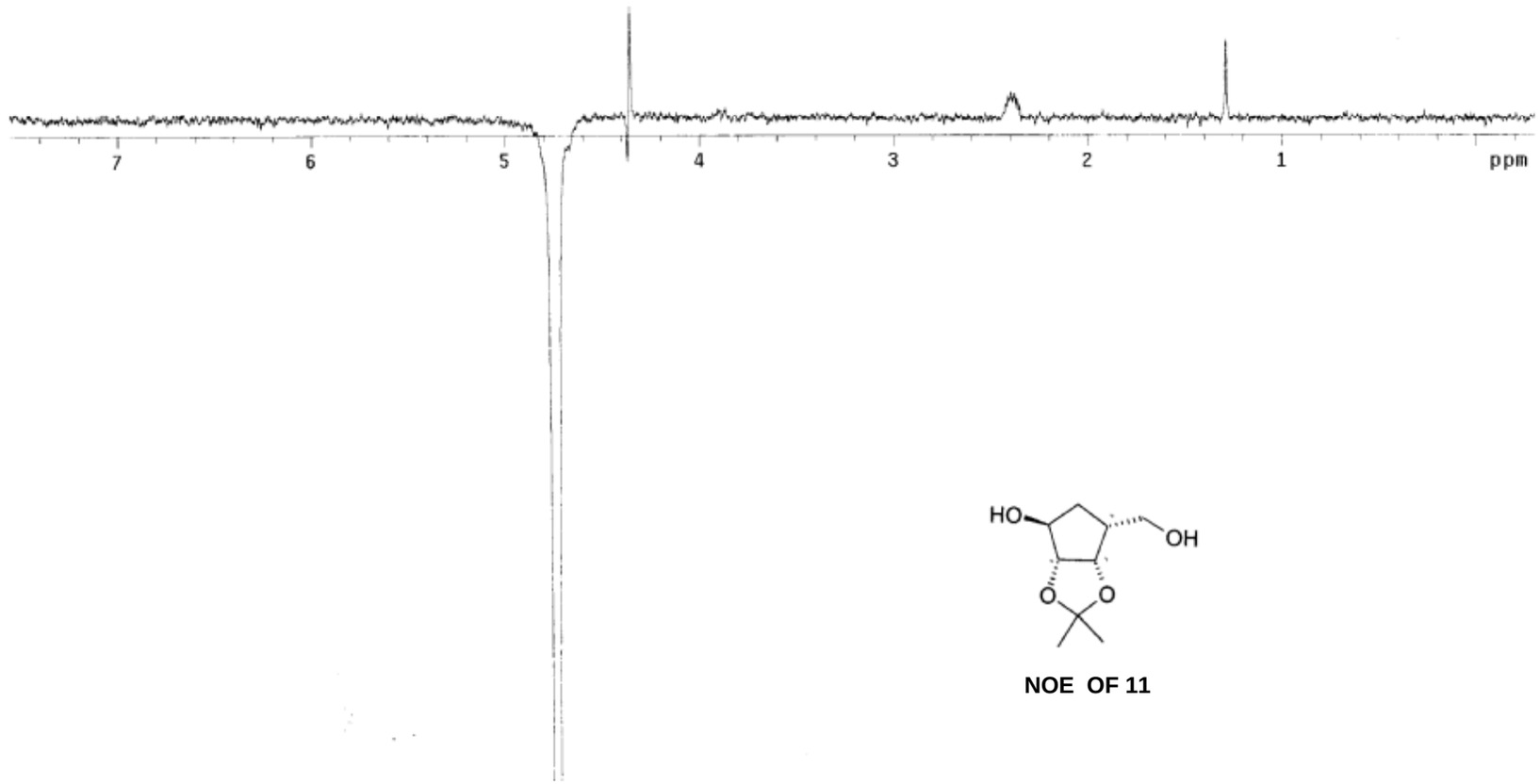
^{1}H NMR OF COMPOUND 11 IN $CDCL_3$ (300 MHz)



^{13}C SPECTRUM OF COMPOUND 11 IN $CDCL_3$(75 MHz)

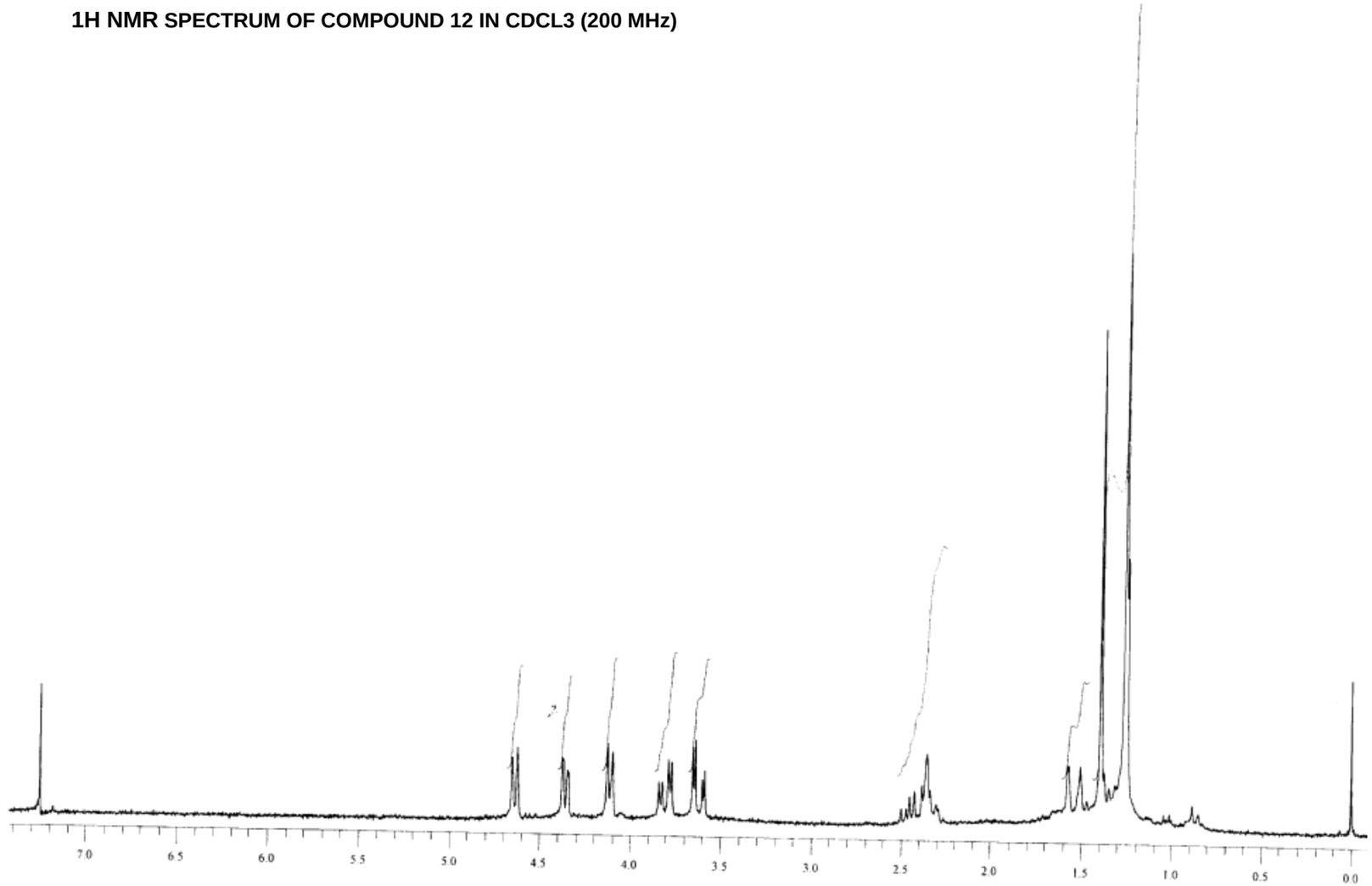


NOE SPECTRUM OF COMPOUND11

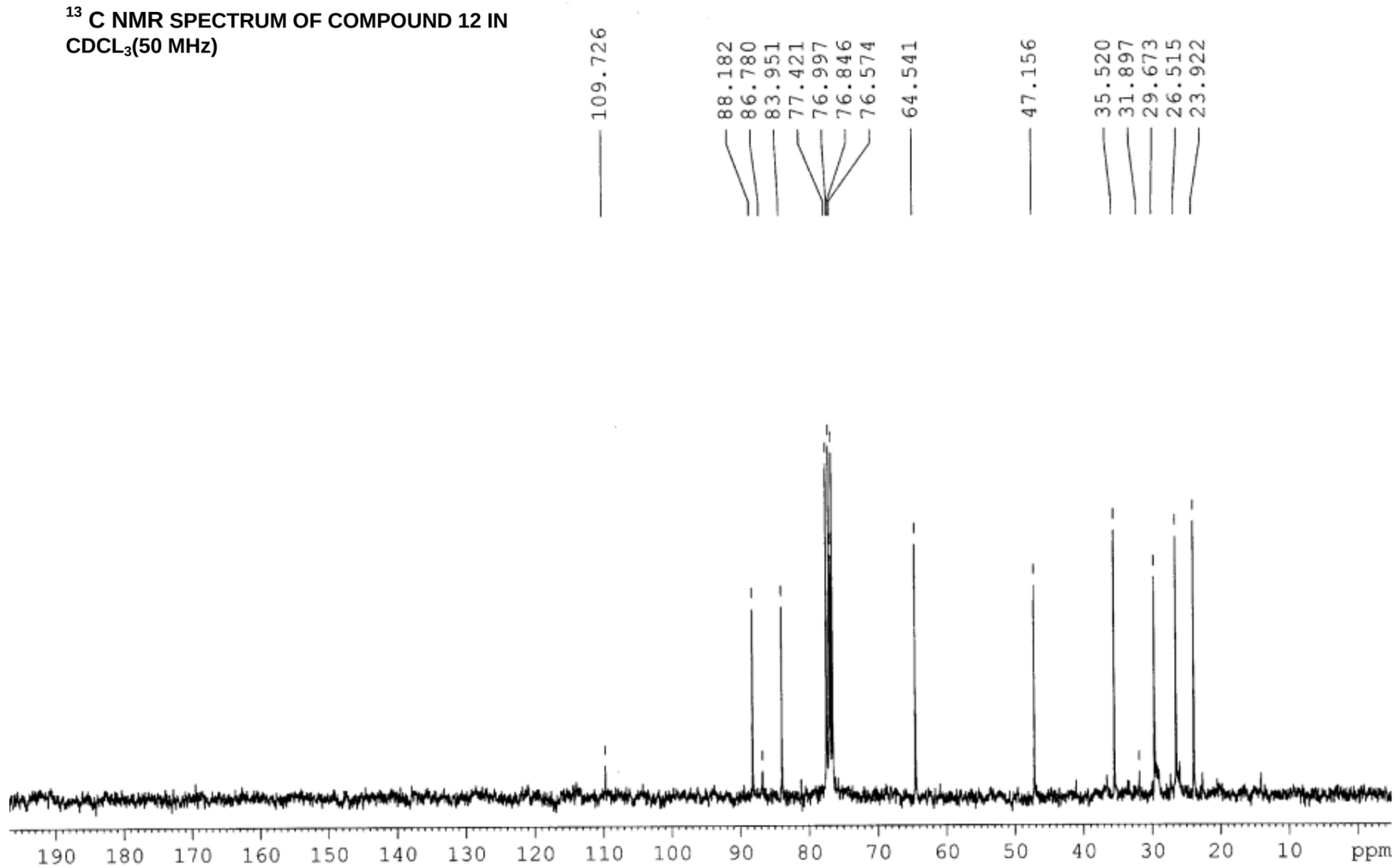


NOE OF 11

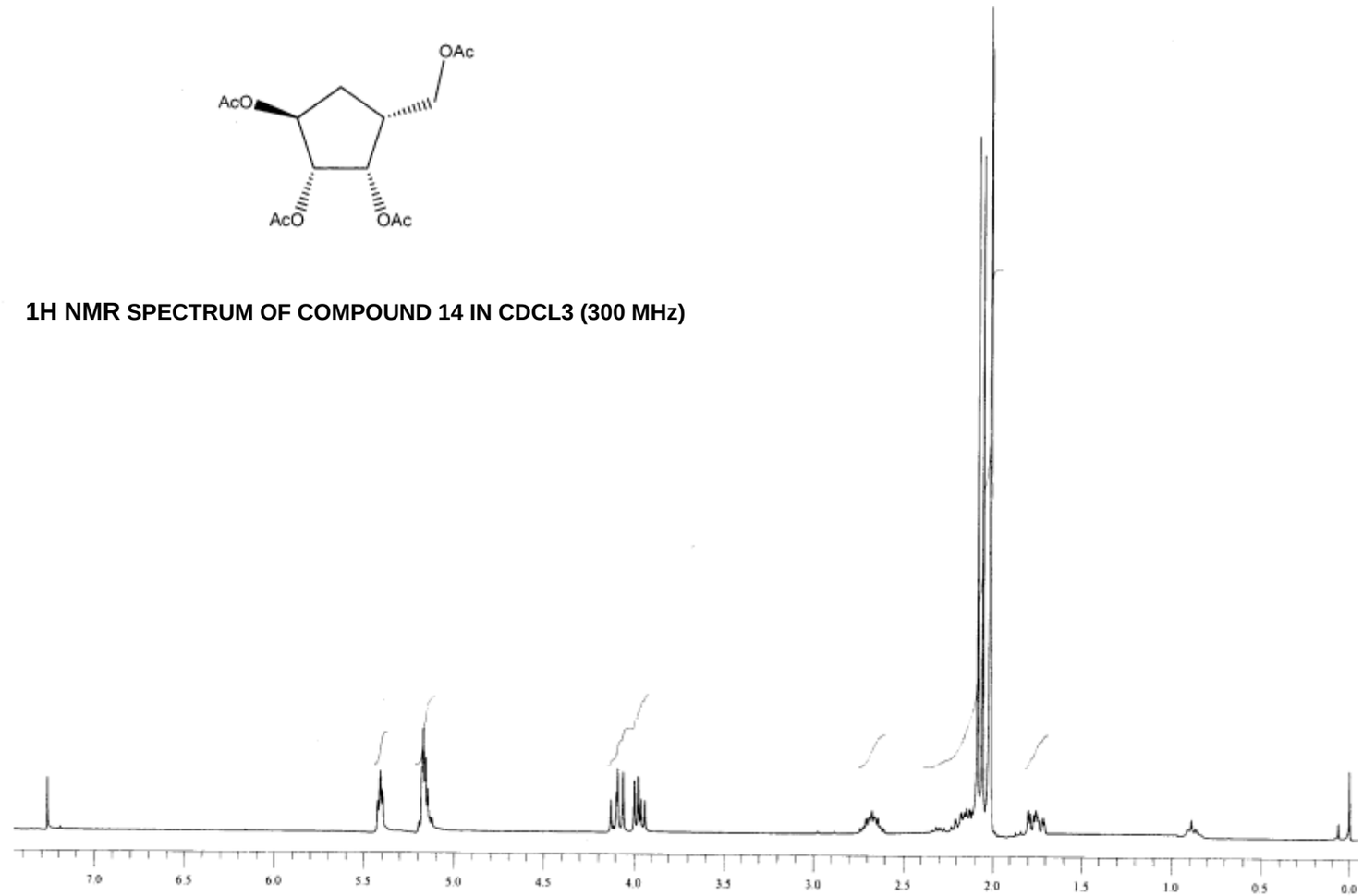
1H NMR SPECTRUM OF COMPOUND 12 IN CDCL3 (200 MHz)



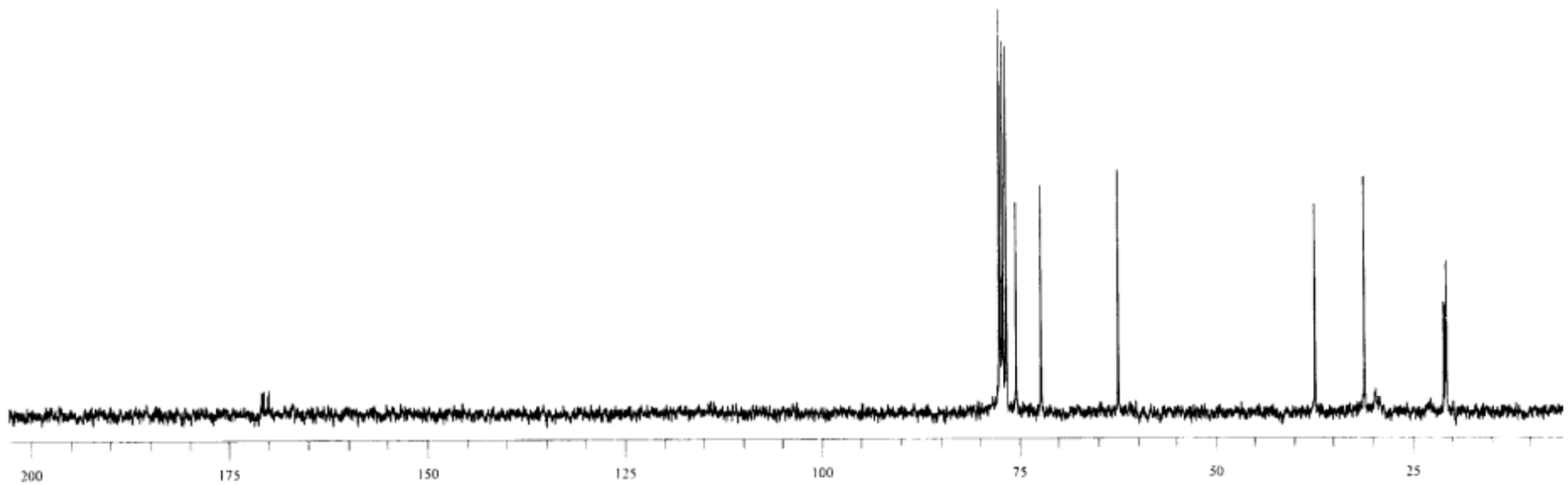
^{13}C NMR SPECTRUM OF COMPOUND 12 IN $CDCL_3$(50 MHz)

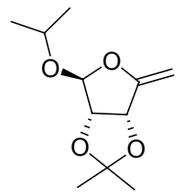


1H NMR SPECTRUM OF COMPOUND 14 IN CDCL3 (300 MHz)



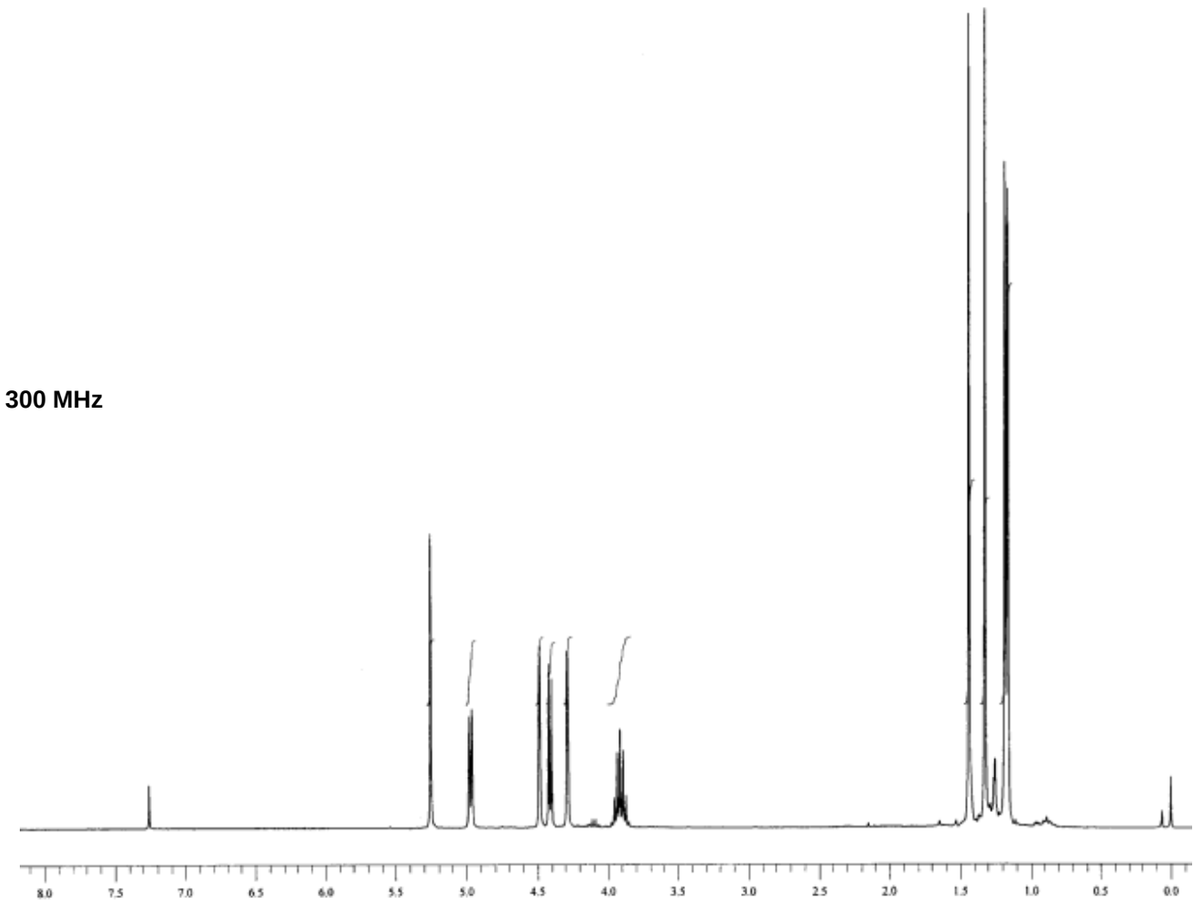
^{13}C NMR SPECTRUM OF COMPOUND 14 IN $CDCl_3$ (75 MHz)

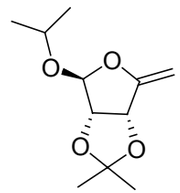


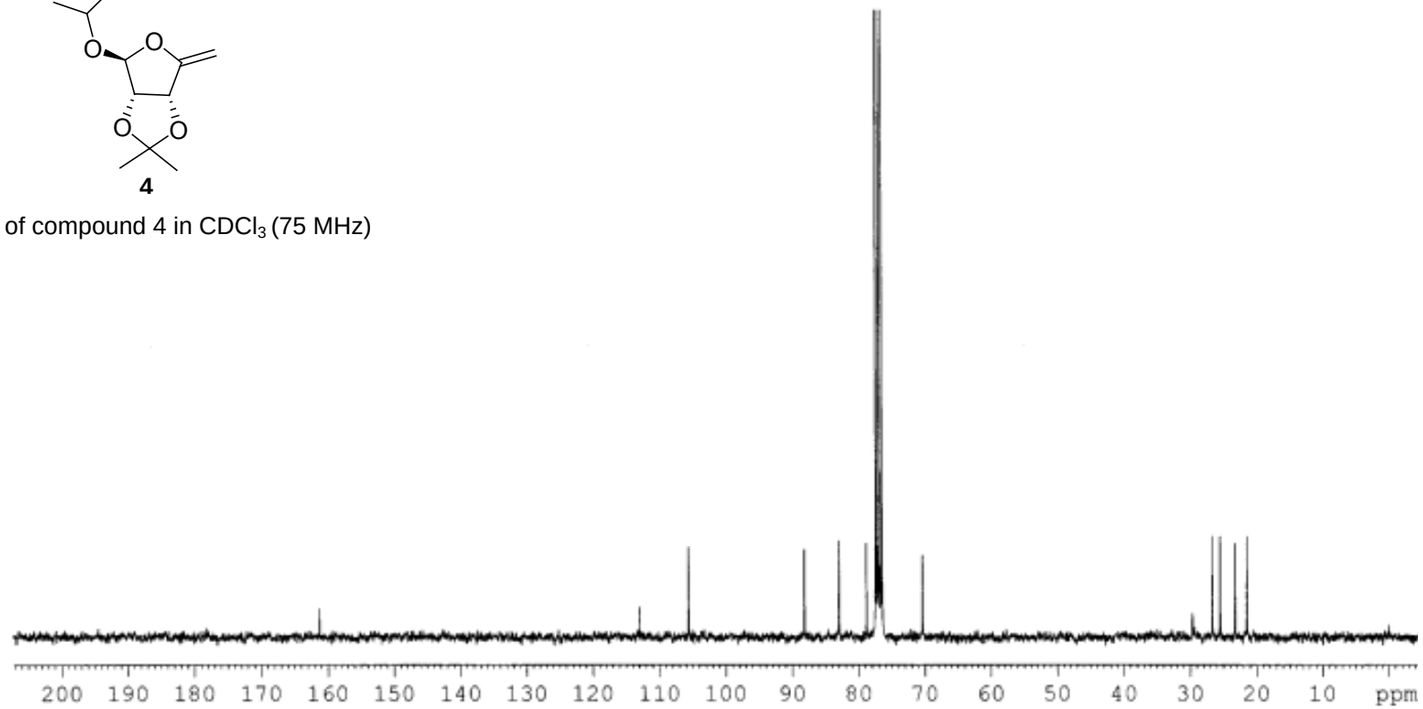


4

^{1}H NMR OF COMPOUND 4 IN 300 MHz





4

C13 NMR of compound 4 in $CDCl_3$ (75 MHz)